



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: R.J. Speirs et al. Attorney Docket No.: CHIR122149  
Application No.: 10/743,529 Group Art Unit: --  
Filed: December 22, 2003 Examiner: --  
Title: METHODS AND UNIT DOSE FORMULATIONS FOR THE INHALATION  
ADMINISTRATION OF AMINOGLYCOSIDE ANTIBIOTICS

DECLARATION OF ARNOLD SMITH, M.D.

Seattle, Washington 98101

TO THE COMMISSIONER FOR PATENTS:

1. I am currently a Member and Principal Investigator at the Seattle Biomedical Research Institute, as well as Professor, Department of Pathobiology, University of Washington, Seattle, WA. My curriculum vitae is attached hereto as Exhibit A.
2. I was an inventor named in a 1994 patent application that issued as U.S. Patent No. 5,508,269 (hereinafter, "the '269 patent").
3. The '269 patent disclosed a treatment method that was approved for clinical use in 1997 under NDA 50-753 (TOBI<sup>®</sup>, Chiron Corporation). According to the attached Exhibit B, the entire TOBI treatment should take approximately 15 minutes to complete.
4. Although such current delivery systems have been shown to be clinically efficacious, they typically suffer from relatively low efficiency levels in delivering antibiotic solutions to the endobronchial space of a patient, thereby wasting a substantial proportion of the nebulized antibiotic formulations and substantially increasing drug delivery costs. The low efficiency of current conventional systems requires patients to devote relatively long time periods to receive an effective dose of the nebulized antibiotic formulations, which can lead to decreased patient compliance.
5. This conundrum is discussed in the '269 patent, in which preliminary laboratory measurements were shown to be uncertain predictors of clinical outcomes.

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6. In particular, the in vitro "Time to Nebulize" measurements listed in Table 1 of the '269 patent did not account for the relative inefficiency in delivering an inhalable mist, and thus were not predictive of actual clinical treatment durations, as illustrated in Exhibit B.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and, further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

April 2, 2004

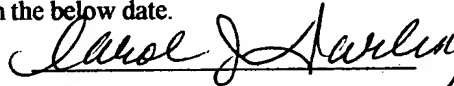


Arnold Smith, M.D.

I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a sealed envelope as first class mail with postage thereon fully prepaid and addressed to Mail Stop ~~Arnold Smith~~ Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the below date.

Date:

June 24, 2004



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